

REMARKS

This is in response to the Office Action dated May 6, 2003. Claims 2-4 have been amended. Claims 1 and 5-13 have been withdrawn from further consideration by the Examiner pursuant to 37 C.F.R. §1.142(b). New claims 14-22 have been added. Claims 2-4 and 14-22 are pending and under consideration.

The specification has been amended to correct typographical errors.

Claims 2-4 have been amended in matters of formal claim language.

New claims 14, 18, 19, and 22 call for a phagocyte-recognizing agent capable of competitive binding or inhibition of a bacteriophages from strain CBS101481 or CBS101482 to a phagocyte or a GM-CSF primed granulocyte. These embodiments are supported by the original specification at, *e.g.*, page 3, lines 7-11 and page 6, line 18 to page 7, line 35.

New claims 15, 20 and 22 call for the phagocyte-recognizing agent comprising a part of an antibody. This is supported by the specification at, *e.g.*, page 5, lines 30-39, and page 10, lines 1-13.

New claims 16 and 21 call for the phagocyte-recognizing agent being a monoclonal antibody. This is supported by the specification at, *e.g.*, page 2, lines 3-5.

New claims 17 calls for the phagocyte-recognizing agent comprising the antigen-specific sequence of a bacteriophage from deposited strain CBS101481 or CBS101482. This is supported throughout the specification, *e.g.*, at page 7, lines 14-35 and page 10, lines 1-9.

No new matter has been added by way of this amendment.

STATEMENT UNDER 37 C.F.R. §1.808

It is hereby stated that the deposit of the microorganisms given the deposit numbers CBS 101481 and CBS 101482 was made under the Budapest Treaty, and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

Enablement

Claims 2-4 stand rejected as allegedly not enabled. Specifically, the Examiner contends that it is not clear that the microorganism is readily available to the public, and that the specification does not enable any phagocyte-recognizing agent recognizing the antigen recognized by at least one bacteriophage isolated from CBS 101481 and CBS 101482. The Examiner also argues that biochemical characteristic of the agent or epitope recognized by the above-cited bacteriophages is not disclosed, that structurally related and unrelated compounds comprising any phagocyte-recognizing agent are not enabled, and cites publications by Colman et al. and Ledman et al. as describing that single amino acid changes can effectively abolish antibody antigen binding; Abaza et al. as teaching that single amino acid substitutions outside the antigenic site on a protein effect antibody binding; and Van Regenmortel as teaching low success rate of antigenic prediction based on continuous epitopes (Office Action, pages 5-6).

In response to the first part of this rejection, a statement pursuant to 37 C.F.R. §1.808, confirming that all restrictions imposed by the depositor on the availability to the public of KCTC 0399BP will be irrevocably removed upon the granting of a patent has been made in this submission (see above).

Applicants respectfully disagree with the second part of the Examiner's rejection, and submit that the present invention as set forth by claims 2-4, as well as by new claims 14-22, is fully enabled by the specification, especially in view of the advanced state of the art. This is particularly evidenced by the fact that the specification, in fact, describes the preparation and screening of a library of ligands, in this case a bacteriophage library, and the successful identification of two bacteriophages which bind to the present antigen on GM-CSF primed granulocytes (see,

specification, page 7, lines 14-38). Using scFv and humanized/monoclonal antibodies made from these bacteriophages, the antigen was retrieved by immunoprecipitation and analyzed by gel electrophoresis (see, specification, page 10, lines 1-22, and Figure 7). Thus, in contrast to the Examiner's reasoning, the possession of a specific ligand to an antigen expressed by a specific set of cells enables the retrieval of the antigen, as well as various binding assays and screening assays for other ligands specific for the same antigen. Such screening or competitive binding assays could be, for example, conducted in a similar manner as the screening assay described in the present disclosure, where a specific cell population expressing the antigen such as GM-CSF primed granulocytes are contacted with a library of agents such as a phage-library (see page 5, line 28, to page 6, line 16) or peptide or combinatorial libraries (see page 3, lines 12-24). Alternatively or additionally, the screening assay could be conducted as a competitive binding assay, screening for agents that compete with either one of the two bacteriophages, as described on page 3, lines 7-11 of the specification. Such competitive binding assays, as well as other or similar forms of screening or binding assays, are, and have long been, well-known in the art.

Thus, while some experimentation may be necessary to enable the invention, no undue or unreasonable experimentation is required for one of skill in the art to practice the full scope of the invention. Specifically, the courts have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required but such experimentation must not be "undue". *Enzo Biochem Inc. v. Calgene, Inc.* 52 USPQ 2d 1129, 1135 (Fed. Cir. 1999) (citing *In re Wands*, 8 USPQ 2d at 1404). The court in *Enzo Biochem* looked favorably on the factors set forth in *In re Wands* to consider in determining whether disclosure requires undue experimentation, some of which were quoted by the Examiner as most relevant to the present invention. These factors are discussed below.

(1) The scope of the claim is enabled given that the specification describes two ligands specific for the antigen to which the phagocyte-recognizing or -binding agent recognizes.

(2) The amount of guidance or direction provided by the specification, in view of the advanced state in the art, is sufficient, given that (a) specific ligands for the antigen are provided,

enabling retrieval and use of the antigen in screening and competitive binding assays, or, indeed, in the production of monoclonal or polyclonal antibodies; (b) specific cell populations, such as GM-CSF primed granulocytes, which express the antigens are described; and (c) the art of binding and competitive binding assays is highly developed;

(3) Working examples of the screening for, identification of, and retrieval of phagocyte-recognizing agents specific for the antigen in question are provided (see page 7, lines 14-35).

(4) Whatever unpredictability there may be in the art regarding which specific amino acids of an antigen are responsible for the binding of a specific agent, these are not relevant for the present invention. In particular, the teachings of the Coleman et al. and Ledman et al. references do nothing to question the enablement of the present invention, since an antibody with an amino acid change abolishing binding to the antigen called for by the claims would not fall within their scope. In this context, the Examiner's attention is respectfully directed to MPEP 2164.08(b), stating "...typically, inoperative embodiments are excluded by the language in a claim (*e.g.*, preamble)...". Accordingly, antibodies or other agents that do not bind to the present antigen would not offend compliance with the enablement requirement, since the present claims call for either binding to the same antigen as the specified bacteriophages or for competitive binding with the same. The teachings of Van Regenmortel are equally irrelevant. While certainly of interest to evaluate the nature of the interaction between a ligand pair, detailed structural information about an antigen such as the 3D-conformation is not needed to prepare or screen for agents that simply bind specifically or competitively to the antigen, as described above.

Accordingly, while some experimentation may thus be required to search for and identify agents binding to the present antigen, such experimentation would not be undue, as it involves routine screening and binding assays exemplified in the present disclosure. This is even more clear with respect to new claims 14-22, which call for phagocyte-recognizing agents characterized by competitive binding with bacteriophages from the deposited strains, as well as specific structural characteristics such as comprising an antigen-binding portion of an antibody (claims 15, 20, and 22), or being a monoclonal antibody (claims 16 and 21).

For all of the above reasons, reconsideration and withdrawal of these enablement rejections is respectfully requested.

Written Description

Claims 2-4 stand rejected as allegedly not complying with the written description requirement. Specifically, the Examiner contends that only two phagocyte-recognizing agents are disclosed by the specification, referring to the bacteriophages from the two deposited strains, and that Applicant is not in possession of *any* phagocyte-recognizing agent.

First, it is respectfully submitted that the Examiner is in err. The specification not only provides the two bacteriophages referenced above, but also discloses scFv fragments as well as humanized antibodies, constructed according to known methods in the art, which recognize the same antigen as the bacteriophages. See page 10, lines 1-9, and Figure 7.

Second, as discussed above, the skilled artisan would readily recognize that being in possession of not only one, but two specific ligand sequences (as well as antibody constructs thereof) to an antigen, as well as a specific cell population expressing the antigen, means that other agents having the same binding specificity are available by routine methods, including high-throughput screening methods as described in the specification on page 2, lines 12-24.

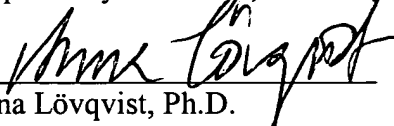
New claims 14-22 also comply with the written description requirement. For example, new claim 17 recite the antigen-binding sequence of the specific bacteriophages isolated from deposited strains CBS101481 and CBS101482 and new claims 15, 16, and 20-22 call for agents comprising the antigen-binding part of an antibody, or the agent being a monoclonal antibody.

For all of the above reasons, reconsideration and withdrawal of this rejection is earnestly solicited.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Dated: November 6, 2003

Respectfully submitted,

By 
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Limited Recognition Under 37 C.F.R.

§10.9(b) (see attached)

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